UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/564,429	04/24/2006	Michael Buschle	SONN:084US/10512512	7323

32425 7590 11/06/2007
FULBRIGHT & JAWORSKI L.L.P.
600 CONGRESS AVE.
SUITE 2400
AUSTIN, TX 78701

EXAMINER	
LUCAS, ZACHARIAH	
ART UNIT	**PAPER NUMBER**
1648	
MAIL DATE	**DELIVERY MODE**
11/06/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/564,429	BUSCHLE ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34,35,39,40,42,45,48,54,58-69,71-73,75 and 76* is/are pending in the application.

4a) Of the above claim(s) *42,45,54,58,59,63,66-69,71 and 75* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34, 35, 39, 40, 48, 60-62, 64, 65, 72, 73, and 76* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 January 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/17/07 5/11/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 34, 35, 39, 40, 42, 45, 48, 54, 58-69, 71-73, 75, and 76 are pending in the application.

Election/Restrictions

2. Applicant's election without traverse of Group I, and the species wherein the hotspot epitopes are those of SEQ ID NOs: 60, 17, and 63, wherein the composition further comprises an immunostimulatory nucleic acid, particularly the ODN of SEQ ID NO: 68, in the reply filed on October 26, 2007 is acknowledged.

3. Claims 42, 45, 54, 58, 59, 63, 66-69, 71, 75, and 76 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions or species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on October 26, 2007.

4. Claims 34, 35, 39, 40, 48, 60-62, 64, 65, 72, and 73 are under consideration.

Information Disclosure Statement

5. The information disclosure statements (IDS) submitted on April 17 and May 11, 2007, are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements have been considered by the examiner.

The following references are in a foreign language accompanied by an English abstract. Due to this, the reference has been examined only to the extent of the disclosure in the abstract.

References B35 and B45 of the April 2007 IDS. .

Reference C1 has not been considered as no English language translation has been provided.

Specification

6. The disclosure is objected to because of the following informalities: It is suggested that the capitalized phrase - - BRIEF DESCRIPTION OF THE DRAWINGS- - be inserted above the description of Figure 1 on page 25, and that the sentence describing the Figure be amended to end with a period.

Appropriate correction is required.

Sequence Listing

7. The specification is objected to for containing referring to sequences without also identifying them by the sequence identifier assigned to them in the sequence listing as required by 37 CFR 1.821(d). In particular, it is noted that the application refers to the deoxy-Inosine/deoxy-Cytosine ODN on page 38 (of the substitute specification of January 11, 2006) as corresponding to SEQ ID NO: 68. However, SEQ ID NO: 68 is represented in the sequence listing a an amino acid sequence comprising a repetition of the sequence isoleucine-cysteine. Thus, the sequence listing does not match the sequence presented in the specification.

The examiner would like to bring the applicant's attention to the following excerpt from MPEP §2422.03:

> 37 CFR 1.821(d) requires the use of the assigned sequence identifier in all instances where the description or claims of a patent application discuss sequences regardless of whether a given sequence is also embedded in the text of the description or claims of an application. This requirement is also intended to permit references, in both the description and claims, to sequences set forth in the "Sequence Listing" by the use of assigned sequence identifiers without repeating the sequence in the text of the description or claims. Sequence identifiers can also be used to discuss and/or claim parts or fragments of a properly presented sequence. For example, language such as "residues 14 to 243 of SEQ ID NO: 23" is permissible and the fragment need not be separately presented in the "Sequence Listing." Where a sequence is embedded in the text of an application, it must be presented in a manner that complies with the requirements of the sequence rules.

The applicant is therefore required to amend the specification to comply with 37 CFR 1.821(d).

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 34, 35, 39, 40, 48, 60-62, 64, 65, 72, and 73 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In making a determination as to whether an application has met the requirements for enablement under 35 U.S.C. 112 ¶ 1, the courts have put forth a series of factors. See, In re Wands, 8 USPQ2d 1400, at 1404 (CAFC 1988); and Ex Parte Forman, 230 U.S.P.Q. 546 (BPAI 1986). The factors that may be considered include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. Id. While it is not essential that every factor be examined in detail, those factors deemed most relevant should be considered.

The present claims are drawn to hepatitis C virus vaccines comprising indicated HCV epitopes. Because the claims read on HCV vaccines, they implicitly require that the claimed

compositions be enabled as providing an effective therapeutic or prophylactic benefit against HCV. In support of the claimed inventions, the application identifies a number of HCV epitopes, and indicates that those in the art would be capable of using such to induce anti-HCV immune responses, including anti-HCV T-cell responses. However, the application does not teach that the claimed compositions were capable of providing a therapeutic benefit against HCV infection.

While the application teaches that the disclosed peptides were capable of inducing T-cell responses, and therefore concludes they would be an effective agent in an anti-HCV vaccine, the art does not support the application's conclusion. In fact, the art teaches that, to date, there are no prophylactic or effective therapeutic treatments against HCV infection. See e.g., Rollier et al. (J Virol 78: 187-96, page 187- of record in the April 2007 IDS); and Huang et al. (Antivir Res 71: 351-62, at 351) (each teaching that there are currently no anti-HCV vaccines, and that the most effective treatments involve compositions not comprising HCV antigens). These references teach that despite years of attempts to develop such a vaccine, those in the art have been hampered from doing so by several difficulties. See e.g., Rollier, at 187; and Berzofsky et al., J Clin Invest 114: 450-62, at 450 and 456-57.

Further, the failure to develop HCV vaccines and therapies have occurred despite the abundance of references through the past 10 years teaching the efficacy of HCV antigens in eliciting humoral and cellular immune response in several infection models. See e.g., Shirai et al., J Virol, 68: 3334-42 (of record in the April 2007 IDS); and Koziel et al., J Virol, 67: 7522-32. Although the art indicates that there has been recent progress in the art (Berzofsky, page 456; and Tan et al., Curr Opin Pharmacol 4: 465-70, at 468), these teachings do not teach that any peptide vaccine would be capable of achieving the claimed results. Rather, the Tan reference

indicates that the most effective vaccines comprise full length E1 or anti-HCV monoclonal antibodies, and that such vaccines have still proven unable to prevent infection. Id. Moreover, even recent teachings in the art indicate that the "determinants of immunity towards HCV are unknown" and indicate that if anti-HCV vaccines are made, they are likely not to be peptides based vaccines. See e.g., Racanelli et al., Clin Immunol 125: 5-12, at pages 6 (left column) and 10 (right column). From these teachings, it would therefore appear that the art of treating and preventing HCV infection is wrought with complexity and unpredictability.

In view of these teachings in the art and the limited teachings in the application with respect to the in vivo and therapeutic activity of the disclosed peptides, the application has not provided sufficient information to enable those in the art to treat and HCV infection with the claimed compositions. Because the compositions do appear to be immunogenic, the claims are rejected as exceeding the scope for which they are enabled to the extent that they read on immunogenic, rather than therapeutic compositions.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 34, 35, 39, and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wentworth et al. (Int Immunol 8:651-59- of record in the April 2007 IDS). These claims are drawn to compositions comprising at least 2 or at least 3 epitopes from the indicated "hotspot

epitopes." It is noted, particularly with respect to SEQ ID NO: 63, that the rejected claims do not require the presence of this sequence per se, but of an epitope found within this sequence.

Wentworth teaches a series of HCV CTL epitopes, and specifically indicates that three of these epitopes were capable of inducing anti-HCV T-cell responses. Pages 654 (Table 4), and 656 (right column). These three epitopes are found in the hotspot epitopes of SEQ ID NOs: 73, 26, and 126 of claim 34, and include the epitopes of SEQ ID NOs: 146 and 85 of claim 39. Moreover, the reference also discloses other epitopes in Table 4 (page 654), including epitopes found in at least 3 of the hotspot epitopes of claim 40, including epitopes found in SEQ ID NOs: 73, 26, and 63 of claim 40. Because the reference indicates that such epitopes are useful for the induction of anti-HCV immune responses, it would have been obvious to those of ordinary skill in the art to make compositions combining the disclosed epitopes. See e.g., MPEP 2144.06 (indicating that it is "*prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose"). Thus, the indicated claims are rendered obvious by the teachings of the Wentworth reference.

12. Claims 34. 35, 39, 40, 48, 60, 62, and 64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Diepolder et al. (J Virol 71: 6011-19- of record in the April 2007 IDS), Cerny et al. (J Clin Invest 95: 521-30), and Lamonaca et al. (Hepatology 30:1088-98- of record in the April 2007 IDS). These claims read on compositions comprising at least two, or at least three, epitopes found within SEQ ID NOs: 60, 63, and 49 (including the elected epitope of SEQ ID NO:. 17).

Each of the three cited references discloses HCV T-cell epitopes, and indicates that the epitopes are useful for the induction of anti-HCV T-cell immune responses. In particular, Diepolder teaches an epitope comprising residues 1248-1261 of the HCV NS3 protein, disclosed as corresponding to SEQ ID NO: 60 (see, page 6014, Figure 3). Cerny teaches an epitope corresponding to SEQ ID NO: 17 of the present application. Page 524, Table II. Lamonaca teaches an epitope found within SEQ ID NO: 63 (the epitope corresponding to SEQ ID NO: 97 of claim 39). Page 1095, Table 3.Because each of these references teaches the epitopes as being anti-HCV T-cell epitopes, and suggests the use thereof for the induction of an anti-HCV immune response, the teachings of these references render the claimed inventions obvious.

13. Claims 39, 48, 61, 64, an d65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Diepolder, Cerny, and Lamonaca as applied to claims 34. 35, 39, 40, 48, 60, 62, and 64 above, and further in view of Wentworth (supra), Day et al. (J Virol 76:12584-595), and Alexander (Human Immunol 59:776-82), and of Van Der Berg (WO 02/70006), Abrams et al. (Cell Immunol 182:137-51), and Chisari et al. (U.S. 2002/0115061). These claims are drawn to compositions described above which comprise the epitope of SEQ ID NO: 63 (disclosed as a hotspot epitope comprising a plurality of epitopes).

As was indicated above, Lamonaca discloses a CD4 epitope found in the sequence of SEQ ID NO: 63. Day discloses two additional CD4 epitopes overlapping with SEQ ID NO: 63. Page 12590, Table 1 (peptides p177 and p178). Further, the teachings of Wentworth (page 654, Table 2), and Alexander (page 778, Table 1) teach CD8/CTL epitopes found within sequence 63 that overlap with, or are nested within the CD4 epitopes identified by Lamonaca and Day.

In addition, Van Der Berg teaches that peptides comprising both CD4 and CD8 epitopes (i.e. CTL and T-helper epitopes) are desirable in the induction of anti-pathogen immune responses. See e.g., page 8. In particular, the reference teaches the use of peptides of 22-35 amino acids in length comprising both CD4 and CD8 epitopes. Abstract. Moreover, Abrams provides similar teachings, and indicates that the CD8 epitopes may overlap, or be nested within, the CD4 epitopes. See e.g., Abstract, pages 138 (right column) and 150 (left column). Other teachings in the art indicate that providing peptides having a plurality of epitopes to account for various alleles would also be beneficial. See e.g., Chisari, page 6, paragraph [0046]. In view of these teachings, it would have been obvious to those of ordinary skill in the art to include in an anti-HCV composition designed to induce an anti-HCV T-cell immune response a peptide comprising the peptide of SEQ ID NO: 63 (potentially with additional C-terminal amino acids in view of the addition amino acids in the epitopes of Day), which sequence those of ordinary skill in the art would have known to a peptide comprising at least one CD4 epitope and at least one overlapping and/or nested CTL epitope.

The combined teachings of the cited references therefore render the claimed invention obvious.

14. Claims 72 and 73 is rejected under 35 U.S.C. 103(a) as being unpatentable over either of Wentworth as applied to claims 34, 35, 39, and 40 above; or of Diepolder, Cerny, and Lamonaca as applied to claims 34. 35, 39, 40, 48, 60, 62, and 64 above, further in view of Schmidt et al. (WO 01/93905- of record in the April 2007 IDS). These claims read on the previously described compositions, further requiring the presence of an immunostimulatory oligodeoxynucleic acid

according to the formula presented in claim 73, particularly wherein the ODN is that referred to in claim 73.

The teachings of the previously applied references have been described above. These references do not teach or suggest the use of the immunostimulatory ODNs of claim 72.

However, the use of such ODNs as adjuvants for peptide based immunogenic compositions was known in the art as shown Schmidt. In particular, this reference teaches ODNs of formula 1 (pages 5-6), and indicates that they may be used as adjuvants for immunogenic compositions comprising any antigen, including peptide antigens. Pages 9-10. The reference specifically indicates that the ODNs may be used as adjuvants for T-cell epitopes (page 10), and as adjuvants for compositions directed against viral, including HCV, antigens (pages 10-11). Furthermore, the reference specifically directs those in the art to polyIC ODNS comprising between 15 and 40 bases in length. Pages 7-8. Thus, the reference directs those in the art to oligo d(IC) molecules of a particular length. The specific molecule of claim 73 represents an immediately recognizable member of this group, and would be obvious both as an obvious member of the group suggested by the reference and as the result of routine optimization of the ODNs suggested by the Schmidt reference.

The combined teachings of these references therefore render the claimed compositions obvious.

15. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Double Patenting

16. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In *re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

17. Claims 34, 35, 36, 4048, 60-62, 64, and 65 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 16-24 of copending Application No. 11/082595. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the present claims, and the claims of the copending application read on anti-HCV immunogenic compositions comprising the epitopes of

SEQ ID NOs: 60, 63, and 17 (corresponding to SEQ ID NOs: 6, 9, and 4 of the copending application). Thus, the present claims represent an obvious embodiment of the copending claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

18. No claims are allowed.

19. The following prior art reference is made of record and considered pertinent to applicant's disclosure. However, while relevant they are also not used as a basis for rejection for the stated reasons.

> U.S. 6,881,723. This reference provides additional recognition that it was known in the art to make immunogenic peptides comprising overlapping T-cell epitopes, including epitopes for different types of T-cells. Columns 6 (lines 1-19), and 10-11 (esp. col. 11, lines 9-18).

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Z. Lucas/
Patent Examiner, AU 1648